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EXAMINER	
ARCHIE, NINA	

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1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/613,736	KRIEG, ARTHUR M.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/12/2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,27-32,43,45,46,50-53,57,63,70-73,76-80,84,88,95 and 97* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☒ Claim(s) *Claims 1-13, 20, 22, 27-32, and 43* is/are allowed.

6)☒ Claim(s) *16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/21/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 14-15, 45-46, 50-53, 57, 63, 70-80, 84, 88, 95, and 97 are withdrawn. .

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 2-12-09. Claims 1-20, 27-32, 43, 45-46, 50-53, 57, 63, 70-73, 76-80, 84, 88, 95, and 97 are pending. Claims 1-13, 16-20, 22, 27-32, and 43 are under examination. Claims 14-15, 45-46, 50-53, 57, 63, 70-80, 84, 88, 95, and 97 are withdrawn. Claims 21, 23-26, 33-42, 44, 47-49, 54-56, 58-62, 64-69, 74-75, 81-83, 85-87, 89-94, 96, and 98 are cancelled.

Rejections Withdrawn

2. In view of the Applicant's amendment and remark following rejections are withdrawn.

a) Rejection of claims 1-13, 17-21, 28-33, and 44 are rejected under 35 U.S.C. 101 is withdrawn in light of applicant's amendment and cancellation of claims (21, 33 and 44).

New Grounds of Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 16-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to a composition, wherein the immunostimulatory nucleic acid has a molecule nucleotide backbone which includes at least one backbone modification (claim 16),

wherein the backbone modification is a phosphorothioate modification (claim 17), wherein the nucleotide backbone is chimeric (claim 18), wherein the nucleotide backbone is entirely modified (claim 19).

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. To adequately describe the genus of nucleotide backbone modifications in an immunostimulatory nucleic acid.

The specification discloses imunnostiumlatory nucleic acid comprising SEQ ID NO: 1 also known as in the art as ODN 10105 (see pgs. 12 and 87). The specification discloses nucleotide backbone modifications (see pg. 4 and 19). The specification discloses various chemical modifications and substitutions (see pg. 16 lines 1-5). The specification does not provide adequate description of the claimed genus of nucleotide backbone modifications in an immunostimulatory nucleic acid.

Applicant has not demonstrated which nucleotide backbone modifications in an immunostimulatory nucleic acid possess the abilities of the claimed immunostimulatory nucleic acid of SEQ ID NO: 1. The limited number of nucleotide backbone modifications in an immunostimulatory nucleic acid disclosed is not deemed to be representative of the genus encompassed by the instant claims. The specification, does not disclose distinguishing and identifying features of a representative number of members of the genus of nucleotide backbone modifications in an immunostimulatory nucleic acid, to which the claims are drawn, such as a correlation between the structure of the nucleotide backbone modifications in an immunostimulatory nucleic acid and its recited function immunostimulatory activity, so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of nucleotide backbone modifications in an immunostimulatory nucleic acid.

Therefore, since the specification fails to adequately describe at least a substantial number of members of the genus of nucleotide backbone modifications in an immunostimulatory nucleic acid aforementioned above to which the claims are based.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing

identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. As evidenced by Yu et al (Yu et al 2001 Biorganic & Medicinal Chemistry Vol. 9 Issue 11 pgs. 2803-2808), whom study the effects of oligonucleotides and structural changes that potentiate or suppress immunostimulatory activities of CpG oligos. Yu et al teach oligonucleotides with no non-ionic linkage showed the ability to induce cell proliferation, however replacing a negatively charged phosphorothioate internucleoside linkage with a non-ionic methylphosphonate linkage resulted in the loss of lymphocyte proliferatory activity (see "Effect of non-ionic internucleoside methylphosphonate linkage in the 5'-flanking sequence" pg. 2804 column 2). Furthermore Yu et al teaches that the non-ionic phosphate linkages may enhance suppress, or maintain immunostimulatory activity compared with an unmodified CpG oligo, depending on the position of the substitution (see pg. 2806 column 1). Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of nucleotide backbone modifications in an immunostimulatory nucleic acid, the skilled artisan could not immediately recognize or distinguish members of the claimed genus aforementioned above. Therefore, because the art is unpredictable, in accordance with the *Guidelines*, the description of the genus of nucleotide backbone modifications in an immunostimulatory nucleic acid is not deemed representative of the genus of a composition comprising a monoclonal antibody to which the claims refer and therefore the claimed invention is not properly disclosed.

Enablement

4. Claims 16-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled for a composition, wherein the immunostimulatory nucleic acid has a molecule nucleotide backbone which includes at least one backbone modification (claim 16), wherein the backbone modification is a phosphorothioate modification (claim 17), wherein the nucleotide backbone is chimeric (claim 18), wherein the nucleotide backbone is entirely modified (claim 19).

Furthermore, the specification does not reasonably enable any composition, wherein the immunostimulatory nucleic acid has a molecule nucleotide backbone which includes at least one backbone modification (claim 16), wherein the backbone modification is a phosphorothioate modification (claim 17), wherein the nucleotide backbone is chimeric (claim 18), wherein the nucleotide backbone is entirely modified (claim 19). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

(A) The nature of the invention;

(B) The breadth of the claims;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Nature of the invention: The instant claims are drawn to a composition, wherein the immunostimulatory nucleic acid has a molecule nucleotide backbone which includes at least one backbone modification (claim 16), wherein the backbone modification is a phosphorothioate

modification (claim 17), wherein the nucleotide backbone is chimeric (claim 18), wherein the nucleotide backbone is entirely modified (claim 19).

Breadth of the claims: The claims encompass any composition comprising SEQ ID NO: 1, wherein the immunostimulatory nucleic acid has any type nucleotide backbone modification which includes at least one backbone modification (claim 16), wherein the backbone modification is a phosphorothioate modification (claim 17), wherein the nucleotide backbone is chimeric (claim 18), wherein the nucleotide backbone is entirely modified (claim 19). Consequently, the instant claims encompass a plethora of defined modification.

Guidance of the specification/The existence of working examples:

The specification discloses imunnostiumlatory nucleic acid comprising SEQ ID NO: 1 also known as in the art as ODN 10105 (see pgs. 12 and 87). The specification discloses nucleotide backbone modifications (see pg. 4 and 19). The specification discloses various chemical modifications and substitutions (see pg. 16 lines 1-5). The specification does not provide adequate description of the claimed genus of nucleotide backbone modifications in an immunostimulatory nucleic acid.

Applicant has not demonstrated which nucleotide backbone modifications in an immunostimulatory nucleic acid possess the abilities of the claimed immunostimulatory nucleic acid of SEQ ID NO: 1. However, the specification is only limited SEQ ID NO: 1. Therefore the data fails to show nucleotide backbone modifications in SEQ ID NO: 1. Therefore, one skilled in the art would not accept on its face the examples given in the specification as being correlative or representative of a successful model. The working examples do not disclose any empirical data or results indicative of a specific backbone modifications (pgs. 80-94).

State of the art: The art indicates Yu et al, whom study the effects of oligonucleotides and structural changes that potentiate or suppress immunostimulatory activities of CpG oligos. Yu et al teach oligonucleotides with no non-ionic linkage showed the ability to induce cell proliferation, however replacing a negatively charged phosphorothioate internucleoside linkage with a non-ionic methylphosphonate linkage resulted in the loss of lymphocyte proliferatory activity (see "Effect of non-ionic internucleoside methylphosphonate linkage in the 5'-flanking sequence" pg. 2804 column 2). Furthermore Yu et al teaches that the non-ionic phosphate

linkages may enhance suppress, or maintain immunostimulatory activity compared with an unmodified CpG oligo, depending on the position of the substitution (see pg. 2806 column 1).

Therefore, the state of the art demonstrates that the effect of a given backbone modification on a given nucleic acid is unpredictable and can only be determined empirically.

In conclusion, the claimed invention is not enabled for any composition any composition comprising SEQ ID NO: 1, wherein the immunostimulatory nucleic acid has any type nucleotide backbone modification which includes at least one backbone modification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention. The specification fails any working examples that disclose any empirical data or results indicative of specific backbone modifications (pgs. 80-94). The state of the art teaches that there are limitations the instant claim aforementioned above thus the state of the art are unpredictable. In view of the lack of support in the art and specification, it would require undue experimentation on the part of the skilled artisan to make and use as claimed; therefore the claims are not enabled. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed composition.

Conclusion

5. Claims 1-13, 20, 22, 27-32, and 43 are allowed.
Claims 16-19 are rejected.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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Nina A Archie
Examiner
GAU 1645
REM 3B31

/Robert A. Zeman/
for Nina Archie, Examiner of Art Unit 1645